

Audit on the uptake of influenza and pneumococcal vaccination in patients with rheumatoid arthritis

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According to the Department of Health guidelines in the UK, patients who are immunosuppressed should be vaccinated against influenza and pneumococcal infection.¹ There are now convincing data regarding the efficacy of vaccination and use of disease-modifying antirheumatic drugs (DMARDs) in patients with rheumatoid arthritis (RA).^{2–5} There is evidence from other countries that the uptake of vaccination is suboptimal, especially in those aged <65 years.⁶

We undertook a study in patients attending our clinics to establish (1) vaccination uptake in our patients who are immunosuppressed, and (2) the reasons if patients had not received the influenza or pneumococcal (pneumovax) vaccination.

We collected data from 155 consecutive patients attending our clinics during March 2006. We enquired about vaccination status during the winter 2005–6 using a questionnaire. We noted whether the patients had received pneumococcal vaccine previously, as this vaccine does not have to be repeated annually. We also noted the diagnosis, current DMARD and glucocorticoid use.

The most common diagnosis was RA (64/155; table 1). DMARDs used were methotrexate (n = 37), sulfasalazine (n = 29), azathioprine (n = 9), prednisolone (n = 10), mycophenolate (n = 3) and tumour necrosis factor α blockade (n = 10); 57 of 155 (37%) patients were not receiving any DMARD or corticosteroids.

Twenty eight (43%) patients with RA had received both influenza and pneumococcal vaccination, 24 (38%) had received neither, 12 (19%) had received influenza vaccination alone, and no patient had received pneumococcal vaccination alone. This was independent of DMARD use. Among the 105 patients with RA and/or taking DMARD, 39 (37%) had received both influenza and pneumococcal vaccine, 24 (23%) had received influenza vaccine only, 2 (2%) had received pneumococcal vaccine only, and 40 (38%) neither.

Influenza vaccination was not received by 24 of 64 patients with RA, the principal reasons being not been offered (5/24), not being old enough (2/24) and for no reason (7/24). Five patients declined vaccination. Pneumococcal vaccination was not received by 36 of 64 patients with RA, because of similar reasons as for not receiving influenza vaccination, except that 5 of 36 patients were not aware of the need for vaccination. Although not specified, the reason for not offering vaccination to these patients might have been their age. There was no single major reason for patients declining vaccination, but offered reasons included fear of vaccination, previous reaction, thought it unnecessary, and this has been noted before.⁵

The vaccination rate in this cohort of patients was sub-optimal, at 37%. This figure is only marginally better than those reported from other countries (20–35%).⁶ The main reason is that patients were not offered vaccination. In the UK, vaccination is routinely offered to people aged >65 years and to those who are immunocompromised. There is a national annual campaign for influenza vaccination every autumn that is coordinated through the computerised age registers maintained in primary care centres. Patients aged <65 years may not be automatically called for vaccination. It is preferable for patients to receive pneumococcal vaccination before starting immunosuppressive therapy, as there is evidence that some patients have a suboptimal response while taking methotrexate.³ This, however, may not always be practicable.

This small audit conducted in a routine rheumatology clinic in the UK suggests that the present strategies for vaccinating patients who are immunocompromised, especially those aged <65 years, is inadequate. We recommend that primary care physicians be educated about the need for vaccination in patients who are taking DMARDs and corticosteroids. Patients should also be educated on the need for vaccination.

Table 1 Patient diagnosis

Diagnosis	n
Rheumatoid arthritis	64
Osteoarthritis	10
Psoriatic arthritis	12
Inflammatory arthritis (not specified)	9
Systemic lupus erythematosus	6
Juvenile idiopathic arthritis	4
Polymyalgia rheumatica	4
Myositis	3
Vasculitis	3
Giant cell arteritis	3
Spondyloarthritis	5
Sjogren's syndrome	3
Myalgia	2
Others	27
Total	155

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REFERENCES

1. PL CMO (2006) 3. The influenza immunisation programme 2006/2007. <http://dh.gov.uk> (accessed 12 Mar 2007).
2. Kapetanovic MC, Saxne T, Nilsson J-A, Geborek P. Influenza vaccination as model for testing immune modulation of anti-TNF and methotrexate therapy in RA patients. *Rheumatology* 2007;**46**:608–11.

Abbreviations: DMARD, disease-modifying antirheumatic drug; RA, rheumatoid arthritis

- 3 Kapetanovic MC, Saxne TT, Sjöholm A. Influence of methotrexate, TNF blockers and prednisolone on antibody responses to pneumococcal vaccine in patients with RA. *Rheumatology* 2006;**45**:106–11.
- 4 Mease PJ, Richlin CT, Martin RW, Gottlieb AB, Baumgartner SW, Burge DJ, et al. Pneumococcal vaccine response in psoriatic arthritis patients during treatment with etanercept. *J Rheumatol* 2004;**31**:1356–61.
- 5 Fomin I, Caspi D, Levy D, Varsan O N, Shalev Y, Paran D, et al. Vaccination against influenza in rheumatoid arthritis: the effect of disease modifying drugs, including TNF alpha blockers. *Ann Rheum Dis* 2006;**65**: 191–4.
- 6 Gluck T. Vaccinate your immunocompromised patients. *Rheumatology* 2006;**45**:9–10.

N-terminal prohormone brain natriuretic peptide: a biomarker for detecting cardiovascular risks in patients with rheumatoid arthritis or osteoarthritis?

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Rheumatoid arthritis (RA) is associated with an increased risk for cardiovascular (CV) events including cardiac insufficiency, acute myocardial infarction and stroke.¹ It is assumed that the release of proinflammatory cytokines and acute-phase proteins furthers the progression of atherosclerosis.^{2–3} This process seems to be further accelerated and aggravated by the administration of cyclooxygenase (Cox) inhibitors (coxibs and non-steroidal anti-inflammatory drugs (NSAIDs)). Therefore, without defining how this could be done, the Food and Drug Administration and European Agency for the Evaluation of Medicinal Products have recommended CV-risk stratification and individualised risk assessment in patients with RA before using coxibs or NSAIDs.

The B type natriuretic peptide (BNP) is a hormone synthesised by cardiomyocytes in response to increased wall tension. The plasma level of its stable, inactive breakdown product, N-terminal prohormone BNP (NT-proBNP), has been identified as a universal predictor of CV risks⁴ even in patients with clinically inapparent impaired CV function. Patients with RA are known to be burdened with an increased incidence of CV impairment.¹ There is preliminary evidence that the serum levels of NT-proBNP in these patients reflect this burden.⁵

Recently, we observed that the use of NSAIDs and coxibs goes along with CV-unwanted drug effects in patients with osteoarthritis (OA) with elevated NT-proBNP values. We analysed the NT-proBNP values in patients with RA (n = 240) and OA (n = 69) and compared the results with those of healthy, age and gender-matched blood donors (n = 2264). We found that patients with RA showed significantly higher NT-proBNP values than matched controls. Moreover, we found a fraction of patients with RA who showed increased NT-proBNP levels without clinical signs of CV dysfunction. We postulate that this fraction comprises a group at risk for CV side effects due to Cox-inhibition.

Patients were recruited from the Department of Rheumatology, Charité University Hospital, Berlin, Germany. The diagnosis of rheumatic diseases was classified according to the American College of Rheumatology criteria. Serum samples were collected after diagnosis and stored deep frozen. Clinical data were documented. We analysed the samples collected from patients at the initial contact.⁶

Besides the few characteristics shown in table 1, the patient cohorts displayed typical distributions of age, sex, autoantibody formation, drug use, and so on. Despite the relatively young

age, patients with RA presented with many CV diseases (table 1).

As in controls, the NT-proBNP levels in patients with RA increased with age and were higher in women than men and altogether higher than in matched controls. But, in contrast with controls (p ≤ 0.01), 39% (table 1) of the patients with RA had NT-proBNP values above the limit of 125 pg/ml. Many of these patients with RA (n = 93) were known to have CV impairments. The diagnosis of (treated) hypertension dominated in the group with low NT-proBNP levels (77%), and the prevalence of coronary artery disease increased from 5% to 30%, with increased NT-proBNP levels. However, almost half of the patients with increased NT-proBNP levels had no apparent signs of impaired CV function (table 1). NT-proBNP values >450 pg/ml are regarded as a serious risk indicator. In our patients with RA, this high limit was exceeded in five women and one man, aged ≥75 years. More importantly, 11 women and 4 men were at lower ages (49–74 years). In other words, 8.8% of the patients with RA presented with high NT-proBNP values, indicating an acute risk of a serious CV event. Of these 21 patients only 10 had symptoms or diagnoses indicating CV dysfunction.

Many of our patients with OA exceeded the limit of 125 pg/ml (49.3%; table 1). However, these patients were >10 years older on average than our patients with RA. Correspondingly, the difference in the NT-proBNP values between patients with OA and controls did not reach significance (table 1). Most of those exceeding the limit of 125 pg/ml had diagnosed CV impairment, often hypertension, but also increased incidence of coronary artery disease (33%). Still several (29%) were without clinical signs of CV impairment. Six patients with OA showed values >450 pg/ml NT-proBNP (8.7%)—one of them without known CV disease. Again, these patients with high NT-proBNP values without CV symptoms might be a specific risk population.

Treatment with Cox inhibitors is frequent in joint disorders and was high in all patient groups (table 1). In this retrospective analysis, most sera were collected before the withdrawal of rofecoxib and valdecoxib, and before special awareness was focused on the use of Cox inhibitors. Thus, the

Abbreviations: Cox, cyclooxygenase; CV, cardiovascular; NSAID, non-steroidal anti-inflammatory drugs; NT-proBNP, N-terminal prohormone natriuretic peptide; RA, rheumatoid arthritis